PTO 08 - 0809

CC= CN
DATE=19971224
KIND=A
PN=1168278

AN ANTINEOPLASTIC TRADITIONAL CHINESE MEDICINE AND ITS PREPARATION METHODS

[一种抗肿瘤的中药制剂及其制备方法]

HU YANKANG

UNITED STATES PATENT AND TRADEMARK OFFICE
WASHINGTON, D.C. NOVEMBER 2007
TRANSLATED BY SCHREIBER TRANSLATIONS, INC.

PUBLICATION COUNTRY	(10):	THE PEOPLE'S REPUBLIC OF CHINA
DOCUMENT NUMBER	(11):	1168728
DOCUMENT KIND	(12):	A
PUBLICATION DATE	(43):	19971224
APPLICATION NUMBER	(21):	96116393.3
APPLICATION DATE	(22):	19960619
INTERNATIONAL CLASSIFICATION	(51):	
PRIORITY COUNTRY	(33):	
PRIORITY NUMBER	(31):	
PRIORITY DATE	(32):	
INVENTOR(S)	(72):	HU YANKANG
APPLICANT(S)	(71):	SHANGHAI DIKANG NUTRIENT AND HEALTHCARE FOOD DEVELOPMENT CO.LTD
DESIGNATED CONTRACTING STATES	(81):	

TITLE (54): AN ANTINEOPLASTIC TRADITIONAL CHINESE MEDICINE AND ITS PREPARATION METHODS

FOREIGN TITLE [54A]: 一种抗肿瘤的中药制剂及其制备方法

Claims

1. An antineoplastics traditional Chinese medicine. Its main feature lies in the fact that it is composed of active parts from traditional Chinese medicine and pharmaceutical necessities, and that the two ingredients can be formulated at any proportion: active parts from traditional Chinese medicine can account for 0.01% - 99.99% (by weight) , while pharmaceutical necessities can be in the range of 99.99% - 0.01% (by weight). The active ingredients include Cochinchina Momordica Seed,chaulmoogra,pangolin,radix et rhizoma rhei, licorice roots northwest origin and caulis bambusae in taenia, to name a few. They can be mixed together to prepare the active ingredients required by the medicine at any dosage of each as follows: cochinchina momordica seed for 5 - 18g, chaulmoogra for 3 - 18g, pangolin for 2 - 6g, radix et rhizome rhei for 5 - 20g, licorice roots northwest origin for l5 - 25g, and caulis bambusae in taenia for 5 - 20g.

2. Preparation methods for the antineoplastics traditional Chinese medicine as described in Claim 1 above. The method is as follows: take subscribed amount of Chinese herb slices, get them grinded to 6 - 8 mesh in fineness, add 3 times volume of ethanol to marinate for 24 hours, heat it and circumfuse for 1 hour, filter, then add 0.6 times volume of the filtered liquid of ethanol for heating and circumfuse for another 1 hour, filter again, and the drug residual be washed with ethanol and squeezed, then combine the twice filtered liquid and the squeezed liquid for filmed condensation. During the condensation process, slowly add 1.3 times volume of ethanol; collect the condensed liquid and recover the ethanol; then depressurize to condense the ethanol content below 4%; add 0.06 times

volume of ethanol that already contains 1% benzoic acid when the liquid is still warm, stir evenly, and cool it down until 18℃, leave it still for 24 hours; separate the solid residuals by centrifugal device; the filtered liquid is then put under 60℃ to warm for 1 hour; stir and cool down before it is finally packaged into a medical mixture, or the filtered liquid may be vacuum condensed to dry ointment by normal methods, then break into fine powders and add excipient and proper amount of 95% ethanol to make into soft ingredient, then add lubricant after cutting and drying. Finally, they are packaged as Chongji, or pressed into tablets, or capsuled.

3. For the said antineoplastics traditional Chinese medicine and its preparation methods in Claims 1 and 2, its pharmaceutical necessities include starch, sugar or syrup as the bond, NaCMC or MCC as disintegrants, ethanol as wetting agent, MS or talcum powder as lubricant, and benzoic acid as preservative.

1

Description

An antineoplastic traditional Chinese medicine and its preparation methods

This invention is in regard of an antineoplastic traditional Chinese medicine and its preparation methods.

Malignant tumor is a serious common disease that endangers people's health and life. According to announcement in 1978 by WHO and its International Center for the Study of Cancer, every year, about 5 million people worldwide died from malignant tumor. In 1992, at the world conference for cancer and AIDS organized by the health agency of the United Nations, it was announced that every year, there had been 9 million new cancer

sufferers in the world, and 6 million people who died from cancer. In 1994, at the Shanghai Forum on the National Prevention of and Drug Study for Chronic Diseases, it was announced that about 1.3 million people died of malignant tumor in whole country, which was only next to fatality due to Cardio - Cerebral - Vascular diseases. Therefore, the treatment of malignant tumor has always been a task of people's key attention. For key modern treatment approaches, there are operation, chemotherapy and radiotherapy, etc. However, all of them have limitations, and there are great toxic side effects from chemotherapy, which usually reduces the white blood cell count, and leads to vomiting, etc. For instance, as recorded in Pages 593 and 294 of 'A New Handbook of Antineoplastic Drugs', published in 1996 by Han Shaoting of Shandong Science & Technology Publishing House, the near - term toxicity of Cyclophosphamide (CTX) is demonstrated by nausea and vomiting, and long - term toxicity is reflected by marrow depression and bleeding bladder infection and hair loss. Over the years, Chinese medicine has been used to treat malignant tumor with certain effects. However, existing Chinese medicine is still not satisfactory in treating stomach cancer, lung cancer and intestine cancer, as well as for the one - year survival line for liver cancer.

The purpose of this invention is to overcome the above deficiencies, by presenting a highly curative antineoplastic traditional Chinese medicine that has low toxicity and side effects.

From research of malignant tumor treatment, the traditional Chinese medicine believes that 'the tumor building is closely related to in - body toxin and dampness heat, stagnancy of blood and qi circulation, phlegm and dampness turbidity, and healthy - qi weakness Vs. evil qi.' Therefore, the tumor remedies are focused on clear - heat and detoxification,

active blood and resolve stasis, resolve phlegm and dissipate stasis, and expel toxin and dissipate binds, etc. For instance, Ping Xiao Tablet, He Chan Tablet, Xiao Zheng Yi Gan Tablet recorded in 'Clinical Instruction for New Chinese and Western Drugs', and the antineoplastic medicines recorded in 'Traditional Chinese Pharmacology' (compiled by Chendu Chinese Medicine Institute) such as Herba Hedyotis Diffusae, Radix Actinidiae Chinensis, Herba Scutellariae Barbatae, cantharides and NIDUS VESPAE (lufengfang), they all have detoxification or toxin - expelling functions.

/2

Based on the above traditional Chinese medicine theories, the inventor intends to expel the toxins, activate blood and dissipate stasis in a way that builds strengths to resolve lumps.

The inventor hereby provides an antineoplastic traditional Chinese medicine (otherwise known as Tiandi Heji), which is composed of active parts from traditional Chinese medicine and pharmaceutical necessities. What's more, the two ingredients can be formulated at any proportion: active parts from traditional Chinese medicine can account for 0.01% - 99.99% (by weight) , while pharmaceutical necessities can be in the range of 99.99% - 0.01% (by weight). The active ingredients include Cochinchina Momordica Seed,chaulmoogra,pangolin,radix et rhizoma rhei, licorice roots northwest origin and caulis bambusae in taenia, to name a few. They can be mixed together to prepare the active ingredients required by the medicine at any dosage of each as follows: cochinchina momordica seed for 5 - 18g, chaulmoogra for 3 - 18g, pangolin for 2 - 6g, radix et rhizome rhei for 5 - 20g, licorice roots northwest origin for 15 - 25g, and caulis bambusae in taenia for 5 - 20g.

The Chinese herbs adopted in this invention have excellent cancer resistant functions.Cochinchina Momordica Seed: bitter in nature, mildly sweet, toxic, able to expel toxins and dissolve binds, good for dispersing of lump in the abdomen; chaulmoogra: hot in nature, toxic, able to expel toxins; pangolin, otherwise known as Manis gigantean: saulty in nature, cool, able to activate blood, expel stasis and dissperse binds, and it can also raise white blood cell counts.Radix et rhizome rhei: bitter in nature, cold, able to activate blood and expel stasis, and resolve stasis and binds. Licorice Roots Northwest Origin: sweet in nature, neutral, able to reinforce the healthy qi, detoxify, work with other drugs, and it is able to neutralize drug toxins and relieve the strength of powerful drugs.

Consequently, the traditional Chinese medicine in this invention highlights expelling both toxins and stasis, which not only dissperses toxins and evil qi, but also resolves binds; the concurrent use of poison and detoxifier, and qi - enhancing ingredient can not only mediate drug potency, but also reinforce the healthy qi and expelling the evil qi; healing, but to the extend not hurting the healthy qi; the appropriate use of mutually supporting ingredients well suits the traditional Chinese medicine theories. Besides, the use of chaulmoogra aims at its toxin - expelling power and heat - dispersing function, so as to support the function of Cochinchina Momordica Seed, which can not only enhance the toxin - expelling effect, but also disperse heats faster, as is an innovative formular for cancer treatment, first of its kind in practice.

The antigeoplastic medicine in this invention (Tiandi Heji) has pharmacodynatics test results as follows:

Part One

I. Purpose of Test

/3

This Test is performed systematically on the transplanted tumor according to requirements by 'the pharmacodynatics studies on the treatment of malignant tumor by using traditional Chinese medicine' in the Pharmacology of 'Research Guidance to New Traditional Chinese Medicine', and a study is made concurrently on its function in enhancing the healthy qi and detoxifying power, so as to illustrate the main curative effects for clinic reference.

II. Medicine tested

Name: Tiandi heji

Provided by: Shanghai Tiankang Pharmaceutical Plant

Labeled Amount: 0.75g crude drug in 1ml

Solvent: 0.5%CMC - Na

Preparation Method: Dilute the original solution with 0.5% CMC - Na to various needed concentration. 0.5ml for each mouse at a time.

III. Animal:

Origin, breed, quality, certificate: BALB/c mouse or F1 (ICR×BALB/c) and Kunming mouse; Animal Group of Shanghai Pharmaceutical Engineering Institute of National

Drug Administration (or known as 'SPEI'); Certificate Number: Hu Dong He Zheng Zi No.l07. (HDHZ Zi No.l07)

C57BL/6 mouse and nude mouse nu/BALB/c are both purchased from Shanghai Lab - Animal Center under Chinese Academy of Sciences. Certificate No.: 'CAS AAA No. 005'.

Weight: 19 ± 1g, 6 - 8 in full age.

Sex: both male and female, adopt the same sex for each time of lab test.

Animal feeding conditions: Kunming mouse: C57BL.6 and Fl mouse are put into clean animal labs. Nude mouse is put into the laminar airflow rack (LAFR), and fed and tested per SPF conditions. All feedstock, cages and drinking water are sterilized. The medicine feeding is conducted within the LAFR.

Various animal counts: three dosages for the tested group.Two groups respectively for Positive comparison and blank comparison. 6 nude mice in each group, Kunming mice, G57BL/6 and F1, 10 in each group.

VI. Selection of Test Method

Mainly to study on the toxin repelling effect, and part of the healthy qi enhancement, detoxification test according to requirements by 'the pharmacodynatics studies on the treatment of malignant tumor by using traditional Chinese medicine' in the Pharmacology of 'Research Guidance to New Traditional Chinese Medicine'.

This product is a traditional Chinese medicine compound, and is tested completely by using whole animals.

/4

V. Main Test Steps:

1. Evil - Qi Repelling

Test on the control of form intestinal cancer C26 transplanted to the animal and Lewis Lung cancer: take relative cancer source under bacteria - free conditions; prepare into even syrup1 - 2×107 tumor cell/ml. Take test mice of the same breed; inject 0.2ml of the tumor cell syrup into each mouse via axil subcutaneous inoculation, or 0.02ml via Subcutaneous injection in the feet toes. Then, they are grouped randomly. The next day, medicine is used per medication plan. After two weeks, anatomize tumor samples from all test groups, and compare them with the comparison group, so as to calculated the control rate.

Per: All items with "***" marks in below tables mean $P < 0.01$; those with "**" marks mean $P<0.05$; and those with "*" mean $P<0.1$.

Table 1 Curative Test on the Form Intestinal Tumor in C - 26 mouse by oral feeding of Tiandi heji.

sample Group No.	dosage mg/kg	drug feeding Plan	animal count beginning (count)end	animal weight beginning (g)end	tumor weight X ± SD	control rate%
Tiandi heji	25	ip×10qd	10 10	19.8 22.7	1.67 ± 0.20	43.87***
Tiandi heji	12.5	ip×10qd	l0 9	19.7 22.6	1.97 ± 0.26	33.78**
Tiandi heji	6.25	ip×10qd	l0 10	19.6 23.1	2.60 ± 0.34	12.6
Positive comparison	30mg					
Cyclophos -	/kg	ip×7qd	l0 10	19.6 20.6	0.30 ± 0.10	89.92***

phamide						
Negative Comparison	Correspond - ing solvent	po×10qd	20 20	19.6 24.7	2.957 ± 0.36	

/5

Table 2 Curative Test on the Form Intestinal Tumor in C - 26 Mouse by Celiac Feeding of Tiandi heji

sample Group No.	dosage mg/kg	drug feeding Plan	animal count beginning (count)end	animal weight beginning (g)end	tumor weight X ± SD	control rate %
Tiandi heji	10	ip×10qd	10 10	18.9 20.6	1.50 ± 0.42	50.82***
Tiandi heji	5	ip×10qd	10 10	19.1 21.2	1.98 ± 0.27	35.08**
Tiandi heji	2.5	ip×10qd	10 10	19.2 21.7	2.35 ± 0.52	22.95
Positive comparison	30mg					
Cyclophos - phamide	/kg	ip×7qd	10 10	19.1 20.4	0.34 ± 0.17	88.85***
Negative comparison	Correspond - ing solvent	po×10qd	20 20	19.1 23.6	3.05 ± 0.29	

Table 3 Curative Test on the feet toes of C - 26 Mouse who has form intestinal cancer by oral feeding of Tiandi heji

sample Group No.	dosage mg/kg	drug feeding Plan	animal count beginning (count)end	animal weight beginning (g)end	tumor weight X ± SD	control rate%
Tiandi heji	25	po×10qd	10 10	19.0 21.0	0.36 ± 0.06	63.96***
Tiandi heji	12.5	po×10qd	10 10	18.8 21.7	0.57 ± 0.08	42.13**
Tiandi heji	6.25	po×10qd	10 10	18.9 21.5	0.79 ± 0.11	19.80
Positive comparison	30mg /kg					
Cyclophos - phamide		ip×7qd	10 10	18.7 20.2	0.29 ± 0.07	70.56***
Negative comparison	Correspond - ing solvent	po×10qd	20 20	18.9 22.0	0.985 ± 0.18	

/6

Table 4 Curative Test on the Feet Toes of C - 26 who has form intestinal cancer by Celiac Feeding of Tiandi heji

sample Group No.	dosage mg/kg	drug feeding Plan	animal count beginning (count)end	animal weight beginning (g)end	tumor weight X ± SD	control rate%
Tiandi heji	10	po×10qd	10 10	19.4 22.9	0.33 ± 0.05	60.71***
Tiandi heji	5	po×10qd	10 10	19.7 22.2	0.45 ± 0.09	46.43***
Tiandi heji	2.5	po×10qd	10 10	19.3 23.7	0.53 ± 0.10	36.90**

Positive comparison	30mg /kg					
Cyclophos - phamide		ip×7qd	10 10	19.5 20.3	0.20 ± 0.05	76.19***
Negative Comparison	Correspond - ing Solvent	po×10qd	20 20	19.5 24.4	0.84 ± 0.08	

Table 5 Curative Test on the Lung Tumor of Lewis Mouse by Oral feeding of Tiandi heji

sample Group No.	dosage mg/kg	drug feeding Plan	animal count beginning (count)end	animal weight beginning (g)end	tumor weight X ± SD	control rate%
Tiandi heji	25	po×10qd	10 10	19.2 21.2	1.63 ± 0.28	43.60***
Tiandi heji	12.5	po×10qd	10 10	19.0 21.7	1.98 ± 0.26	31.49***
Tiandi heji	6.25	po×10qd	10 10	19.3 21.3	2.33 ± 0.38	19.38
Positive comparison	30mg					
Cyclophos - phamide	/kg	ip×7qd	10 10	19.1 20.4	0.32 ± 0.10	88.93***
Negative Comparison	Correspond - ing solvent	po×10qd	20 20	19.1 23.1	2.89 ± 0.31	

/6

Table 6 Curative Test on the Lung Tumor of Lewis Mouse by Celiac Feeding of Tiandi heji

sample Group No.	dosage mg/kg	drug feeding Plan	animal count beginning (count)end	animal weight beginning (g)end	tumor weight X ± SD	control rate%
Tiandi heji	10	po×10qd	10 10	19.1 20.5	1.48 ± 0.26	45.39***
Tiandi heji	5	po×10qd	10 9	19.0 21.1	1.83 ± 0.26	32.47**
Tiandi heji	2.5	po×10qd	10 10	18.7 21.7	2.24 ± 0.25	17.34
Positive comparison	30mg					
Cyclophos - phamide	/kg	ip×7qd	10 10	18.9 20.3	0.22 ± 0.06	91.88.***
Negative Comparison	Corres pond - ing solvent	po×10qd	20 19	19.0 22.6	2.71 ± 0.37	

Same methods for the test on human tumor xenotransplantation model MKNand QGY. However, all tests must be operated and drug - fed under the strict sterilized conditions.

Table 7 Curative Test on Human Liver Cancer QGY by Oral Feeding of Tiandi heji

sample	dosage	drug	animal	animal	tumor	control

Group No.	mg/kg	feeding Plan	count beginning (count)end	weight beginning (g)end	weight X ± SD	rate%
Tiandi heji	25	po×10qd	6 6	17.4 17.3	1.12 ± 0.15	47.91***
Tiandi heji	12.5	po×10qd	6 6	17.7 18.8	1.45 ± 0.31	32.56**
Tiandi heji	6.25	po×10qd	6 6	17.3 18.5	1.73 ± 0.51	20.00
Positive comparison	30mg					
Cyclophos - phamide	/kg	ip×7qd	6 6	17.6 18.4	0.32 ± 0.17	85.12***
Negative Comparison	Correspond - ing solvent	po×10qd	12 12	17.5 20.5	2.15 ± 0.32	

/7

Table 8 Curative Test on Human Live Tumor QGY by Celiac Feeding of Tiandi heji

sample Group No.	dosage mg/kg	drug feeding Plan	animal count beginning (count)end	animal weight beginning (g)end	tumor weight X ± SD	control rate%
Tiandi heji	10	ip×10qd	10 6	18.8 17.3	0.97 ± 0.42	48.96***
Tiandi heji	5	ip×10qd	10 6	18.7 17.7	1.27 ± 0.37	33.85**
Tiandi heji	2.5	ip×10qd	10 6	18.6 17.9	1.72 ± 0.51	20.00
Positive comparison	30mg					
Cyclophos - phamide	/kg	ip×7qd	10 6	18.5 17.0	0.27 ± 0.05	85.93***
Negative Comparison	Correspond - ing solvent	ip×10qd	12 12	18.8 20.8	1.92 ± 0.36	

Table 9 Curative Test on Human Stomach Cancer by oral feeding of Tiandi heji

sample Group No.	dosage mg/kg	drug feeding Plan	animal count beginning (count)end	animal weight beginning (g)end	tumor weight X ± SD	control rate%
Tiandi heji	25	ip×10qd	6 6	17.4 16.0	0.27 ± 0.04	86.76***
Tiandi heji	12.5	ip×10qd	6 6	17.6 17.5	0.83 ± 0.36	59.31**
Tiandi heji	6.25	ip×10qd	6 6	17.9 18.9	1.65 ± 0.40	19.12
Positive comparison	30mg					
Cyclophos - phamide	/kg	ip×7qd	6 6	17.7 16.8	0.14 ± 0.04	93.14***
Negative Comparison	Correspond - ing solvent	ip×10qd	12 12	17.9 19.4	2.04 ± 0.19	

/8

Table 10 Curative Test on Human Stomach Cancer MKN by Celiac Feeding of Tiandi heji

sample Group No.	dosage mg/kg	drug feeding Plan	animal count beginning (count)end	animal weight beginning (g)end	tumor weight X ± SD	control rate%
Tiandi heji	10	po×10qd	6 6	18.2 15.6	0.175 ± 0.04	85.42***
Tiandi heji	5	po×10qd	6 6	18.4 16.6	0.45 ± 0.14	62.50**
Tiandi heji	2.5	po×10qd	6 6	18.3 17.8	0.70 ± 0.14	41.67***
Positive comparison	30mg					
Cyclophos - phamide	/kg	ip×7qd	6 6	18.4 16.8	0.12 ± 0.05	90.00***
Negative Comparison	Correspond - ing solvent	po×10qd	12 12	18.4 19.1	1.20 ± 0.29	

2. Enhance the Healthy Qi

(1) Tiandi heji's effect in Phagocytic Function of peritoneal macrophages of various normal Kunming mice: take a few male Kunming mice for random grouping, 10 in each group. For oral feeding, once a day for 10 days on end. After the last feeding, intraperitoneal injection of 1.5ml 0.5% protein hydrolysate into each mouse in all groups. After 24 hours, intraperitoneal injection of 0.2ml 1x106 /ml chicken red blood cell syrup into each mouse, and wait for 40 minutes. Then collect celiac fluid by using normal saline, and obtain centrifugally the cell precipitation sap to make into plates, which is fixed carbinol, tinted by Miemsa Method, and then sealed. Use the oil lens to respectively count the number of macrophages in chicken's red blood cells and the number of red blood cells that are swollen by l00 macrophages. Use the following formula to calculate the phagocytosis percentage and index.

Number of macrophage in chicken's red blood cell swollen by 100 macrophages

$$\text{Phagocytosis percentage} = \frac{\text{100 macrophage}}{\text{Total number of chicken red blood cells swollen by 100 macrophages}} \times 100\%$$

$$\text{Phagocytosis index} = \frac{\text{100 macrophages}}{\text{/10}} \times 100\%$$

(2)Tiandi heji's impact on the activity of Lewis Lung Cancer bearing mouse NK: Take C57BL/6 mouse, and conduct hypodermic injection of 4 - $5x10^6$ Lewis Lung Cancer even cell syrup into its right foot toe. Starting the next day, to treat with Tiandi heji per 12.5, 6.25 and 3.125ml/kg po×7qd plans. After drug feeding, kill all groups of animals, and take out the spleens under bacteria - free conditions. Separate out the spleen cells for 1×10^7/ml effector cells. Take the Yac - 1 cells that are cultivated as target cells, with concentration of 1×10^6/ml. Take 100μl of each of the above cells to add into the 96 - hole board, and then add 3H - TdR 1.75×10^4Bq per hole to develop for 24 hours. To collect cells with fine collectors, and test cmp value in each hole under the Liquid Scintillation Counter. Finally test and mark significant differences between various testing groups and the comparison group.

Table 11 Tiandi heji's Impact on Tumor - Bearing Animal NK

sample Group	dosage mg/kg	Drug - feeding Plan	CPM X ± SD
Tiandi heji	12.5	po×10qd	4218 ± 736**
Tiandi heji	6.25	po×10qd	5531 ± 1043*
Tiandi heji	3.125	po×10qd	4312 ± 671**
Tiandi heji		po×10qd	6004 ± 916
Tiandi heji	12.5	po×10qd	3631 ± 554**
Tiandi heji	6.25	po×10qd	3153 ± 911**
Tiandi heji	3.125	po×10qd	3729 ±

			1144**
Comparison		po×10qd	4941 ± 873

3. Potency - Enhancing Function: take Kunming breed mouse, inject even syrup of S180 tumor via oxter subcutaneous inoculation. The next day, to group them per Tiandi heji 26.0, 12.5 and 6.25ml/kg po×10 for independent group and merged group. To add 15ml/kg Cyclophosphamide ipx7 into all three Tiandi heji. 12 days after the tumor is transplanted, to obtain tumors in all groups, get the average value and SD of tumors in all groups, and compare them with the comparison group to calculate the tumor control rate.

/11

Table l2 Curative Effect on S180 by Tiandi heji combined with Cyclophosphamide

sample Group	dosage mg/kg	Drug - eeding Plan	tumor weight X ± SD	control rate%
Tiandi heji	25.0	po×10	1.21 ± 0.35	60.97***
Tiandi heji	12.5	po×10	1.73 ± 0.3	44.19***
Tiandi heji	6.25	po×10	2.25 ± 0.28	27.42***
Tiandi heji	25.0	po×10	0.89 ± 0.3	71.29***
CT X	15.0mg/kg	ip×7		
Tiandi heji	12.5	po×10	1.56 ± 0.39	49.68***
CT X	15.0mg/kg	ip×7		
Tiandi heji	6.25	po×10	1.82 ± 0.25	41.29***
XT X	30.0mg/kg	ip×7		
CT X	15.0mg/kg	ip×7	1.70 ± 0.26	45.16***
CT X	15.0mg/kg	ip×7	0.48 ± 0.11	84.52***
comparison	Corresponding solvent	po×10	3.10 ± 0.46	
comparison	Corresponding solvent	po×10		

4. Detoxification Function: Take F1 mouse of BALB/c x IGR, lab - use Cyclophosphamide l00mg/kg ip x 2, then have random grouping. Set up three test groups, respectively for Tiandi heji 25.0, 12.5 and 6.25ml/kg po×10qd. Then, test the white cell every 4 days, and obtain the RSD average value in each group. Take Day 0's white cell for 100%, to calculate the percentage rate of white cells at all times.

VI. Dosage Design

/12

The dosage for high, medium and low levels of P0 is respectively 25.0, 12.5 and 6.25ml/kg; the dosage for high, medium and low levels of ip is respectively 10.0, 5.0 and 2.5ml/kg.

VII. Method of Drug Feeding

Evil - qi repelling, healthy - qi enhancement, potency strengthening and detoxification functions are demonstrated by PO xl0qD and ip×10qd, and oral feeding is the clinic drug - taking approach. The healthy - qi enhancing function is only as PO approach, and it is tested per 12.5, 6.25 and 3.125ml/kg po×10 scenario.

VIII.Test Comparison

Blank Comparison: corresponding solvent: 0.5%CMC - Na.

Positive drug comparison: as it is a traditional Chinese medicine compound, there is no proper positive comparison, therefore, the regular Cyclophosphamide is adopted to prove the reliability of each test.

IX. Test Result

1. Evil - Qi Repelling Function: as in - body tumor - resisting test shows, Tiandi heji has a high control rate on the high - dosage 25ml/kgpo×l0 of human stomach cancer exnotransplantation model MKN and l0ml/kg ip×10. The control rate respectively reached 74.68 - 86.76% and 78.72 - 85.42%. According to the national standard, a tumor control rate above 30% shall be deemed effective (per Page 104 of the 'Research

Guidance on New Traditional Chinese Medicines' issued by the Pharmaceutical Administration of the Ministry of Health).Meanwhile, medium dosage groups for 12.5ml/kg po×10 and 5ml/kg ip x l0 have also demonstrated a medium level tumor control rate, which respectively proved at 49.86 - 59.31% and 55.32 - 62.5%. For the other three animal transplanted tumors, i.e.C26 (via two hypodermic injection ways through arm and feet toe) , Lewis Lung Cancer and human liver cancer exnotransplantation model QGY, the two drug - feeding ways have shown medium level tumor control effects. The medium - dosage group demonstrates a verge control rate. The celiac approach is a bit more effective than the oral approach. As proven by main pharmacodynamics, Tiandi heji has an obvious function in expelling the evil - qi (see Table 1 - 10).

2. Healthy - qi enhancement: It can obviously promote the phagocytosis function of the mouse's peritoneal macrophages, and can improve to some extent the activity of the NK cells in the mouse who is bearing Lewis lung cancer.

See table 11).

3. Detoxification Function: there is no obvious role in raising the white cell counts that are affected by Cyclophosphamide, nor did it appear to have any restriction on the addition of the white cell counts. (See Table 13)

4. Potency - Increase: High dosage of Tiandi heji combined with low dosage of Cyclophosphamide will obviously enhance the potency of S180.(see table 12)

/13

Table 13 Detoxification Test Result of Tiandi heji on Lowered Counts of White Cells by Cyclophosphamide

sample Group	dosage mg/kg	Drug - feeding Plan	white cell percentage rate Vs Day 0f or 100%					
			Day 0	Day 3	Day 6	Day 9	Day 12	Day 15
Tiandi heji	25.0	pox10qd	100	37.5	44.5	55.0	66.0	99.0
Tiandi heji	12.5	pox10qd	100	35.6	41.6	53.9	63.2	98.5
Tiandi heji	6.25	pox10qd	100	36.0	43.1	50.5	62.7	102.4
Correspond - ing solvent		pox10qd	100	33.6	43.0	47.2	57.8	92.9

Part Two

The in - body Tumor - resistance test by the antigeoplastic traditional Chinese medicine in this invention (i.e.Tiandi heji)

I.Purpose of Test

To observe the control of tumor growth by Tiandi heji regarding mice thathave been transplanted with tumor S - 180 and liver tumorHzz through oral drug taking, so as to learn the tumor - resisting effect by Tiandi Heji.

II. Tested Medicine

Name: Tiandi heji

Provided by: Shanghai Tiankang Pharmaceutical Plant

Labeled Amount: 0.75 crude drug in 1ml.

Method of preparation: use the original solvent for dilution.

Solvent: N/A

III. Animal: white mouse

Source: Shanghai Lab Test Animal Center under Chinese Academy of Science, Kunming Breed. CAS Shanghai N - 94Q.

Weight:18—22g(6 full age) both female and male.

Animal quantity: 360g, and 10 in each group.

/14

IV. Selection of Test Method

According to the New Drug (traditional Chinese medicine) Research Guidance, to select more than two testing methods: option one, mouse transplanted tumor S - 180 and liver tumorHzz for in - body tumor resistance test; option two, obtain cell strains from human cervical cancer Hela, human liver cancer 7704, human stomach cancer 7901 and human lung adenoidal cancer A1 for off - body tumor resistance test.

V. Main Test Steps:

Slice the long - term preserved tumor S - 180 and liver tumorHzz into small bits in the size of 2x2mm in the super clean platform, and use sleeve pipe needle to conduct arm hypodermic injection into the mouse. The next day, to randomly group the animals, 10 in each group. Then to feed different dosages of Tiandi Heji through stomach lavaging (ig), or the comparison feeds. Once a day, for 7 days on end. Kill the animals within 24 hours once the drug feeding is completed. Weigh them, anatomize to separate the tumor for weighing. Use the following formula to calculate the tumor growth control rate:

$$\text{Tumor growth control rate} = \frac{\text{Comparison group tumor weight} - \text{curing group tumor weight}}{\text{Comparison group tumor weight}} \times 100\%$$

At the same time, to conduct T test with a computer, and compare if there is any significant difference between the curing group and the comparison group.

VI. Test on tumor control rate: the average tumor weight in comparison group >1g; the average weight of animals in the curing group is reduced by <15%; the fatality rate in each group is less than 20%; tumor weight control rate is above 30%, which is obviously different from the comparison group.

VII. Reactions of Animals after drug - feeding

Quiet, inactive.

VIII. Observation time: once a day

IX. Dosage Design

Tiandi heji is a traditional Chinese medicine compound. At the very beginning of the test, it demonstrated that 30ml/kg(10.6m1/20g),ig did not show any toxic reaction. Therefore, three dosage groups, i.e.high, medium and low, are set up respectively for 25.0, 17.5 and 10.0ml/kg for curative effect observation.

dosage labeling method: ml/kg.

X. Drug - feeding method

/15

For blank comparison group, they use normal saline (0.9%NS).

The drug - feeding approach is the same as for clinic oral taking way. Mouse stomach lavaging (ig).

Drug - feeding times: once a day (ig), for 7 days on end.

XI. Test Comparison

For blank comparison group, they use normal saline (0.9%NS)

For known positive comparison group, to select Pingxiao Capsule, which is another traditional Chinese medicine compound already in clinical use, and produced by Shaanxi Xian State Pharmaceutical Plant under the supervision of China Anti - Cancer Association, with license of Shaan Wei Yao Zun Zi (1984) 00201, and provided by Shanghai Tumor Hospital. Use 0.5%CMC distilled water to prepare 0.4g/ml solution.

Besides, use FLUOROURACIL SUPPOSITORY (5 - Fu) , O.25g/10ml per Ampoule bottle, produced by Shanghai Haipu Pharmaceutical Plant, batch number: 9308581, provided by Shanghai Tumor Hospital.

Ping Xiao Capsule selects a maximum toxic - free and acceptable dosage of 4g/kg, while 5 - Fu selects a normally effective dosage of 40mg/kg for tumor - control.

XII. Result

Tiandi heji has certain effects in controlling the growth of flesh tumor (S - 180) and liver tumor (HZZ). The continuous three tests showed similar results, and demonstrated a good dosage - effect relationship. It shows a significant difference from the NS comparison group, with $P<0.01$. It is quite close to FLUOROURACIL SUPPOSITORY (5 - Fu) group. See Tables 14 and 15. Dosages of Tiandi heji at 17.5 and 25.0ml/kg respectively shows a control rate of 33.0% and 40% on S - 180; and their control rate on Hzz is respectively at 35.6% and 44.2%. 5 - Fu40mg/kg has a tumor control rate of 44.8% and 51.9% respectively on S - 180 and Hzz. Ping Xiao Capsule of 4g/kg has a tumor control rate of 17.6% and 24% respectively on S - 180 and Hzz.

/16

Table 14 Tumor Control Rate (n = 3) by Tiandi heji on S - 180

drug	dosage×days	drug feeding	count	average tumor	tumor weight	P value

		way		weight ± SD	control rate	
NS	10.0ml/kg×7	ig	30	2.10 ± 0.5	/	/
Tiandi heji	10.0ml/kg×7	ig	30	1.59 ± 0.49	24.3%	> 0.05
Tiandi heji	17.5ml/kg×7	ig	30	1.40 ± 0.49	33.3%	> 0.05
Tiandi heji	25.0ml/kg×7	ig	30	1.26 ± 0.37	40.0%	> 0.01
Ping Xiao Capsule	4g/kg×7	ig	30	1.73 ± 0.53	17.6%	> 0.05
5 - Fu	40mgl/kg×7	ig	30	1.16 ± 0.34	44.8	> 0.01

Average P value Vs NS Group

Table 15 Tumor Control Rate (n = 3) by Tiandi heji onHzz

drug	dosage×days	drug feeding way	count	average tumor weight ± SD	tumor weight control rate	P value
NS	10.0ml/kg×7	ig	30	2.08 ± 0.66	/	/
Tiandi heji	10.0ml/kg×7	ig	30	1.60 ± 0.63	24.3%	> 0.05
Tiandi heji	17.5ml/kg×7	ig	30	1.34 ± 0.44	35.6%	> 0.05
Tiandi heji	25.0ml/kg×7	ig	30	1.16 ± 0.52	44.2%	> 0.01
Ping Xiao Capsule	4g/kg×7	ig	30	1.62 ± 0.40	24.0%	> 0.05
5 - Fu	40mgl/kg×7	ig	30	1.01 ± 0.58	51.9	> 0.01

Average P value Vs NS Comparison Group

Conduct mouse stomach lavaging by Tiandi heji at 17.5 and 25.0ml/kg for seven days on end, then it shows certain control on the growth of tumor (S - 180) and liver tumor (H_{22}). The effect is better than Ping Xiao Capsule, but close to that of 5 - Fu.

Part Three Tests

/17

Off - Body Tumor - Resistance Test by the antigeoplastic traditional Chinese medicine in this invention (Tiandi heji) :

I.Purpose of Test

To observe the tumor control function of the antineoplastic drug, i.e.Tiandi heji on common malignant tumor cells that are cultivated out of the human body, such as human cervical cancer Hela, liver cancer 7704, stomach cancer 7901 and human lung adenoidal cancer A1

II.Tested Medicine

Name: Tiandi heji

Provided by: Shanghai Tiankang Pharmaceutical Plant

Labeled Amount: 0.75g crude drug per ml.

Preparation method: dissolved in the cultivation medium that contains 15% calf serum.

Preparation for use at any time.

Cell strains:

1.Human liver cancer cell strain (7704).

2.Human stomach cancer cell strain (7901).

3.Human lung adenoidal cancer cell strain (A1).

4.Human cervical cancer cell strain (Hela).

Source: Shanghai Cell Institute Cell Storage under Chinese Academy of Sciences

III.Selection of Test Method.

Test of Off - Body tumor resistance

IV.Main Testing Steps

Collect the tumor cells from DMEM cultivation medium plus 15% calf serum, count the quantity, then put them into cell cultivation bottles per 130000/bottle.

Add different dosages of testing drugs into the cultivation bottles with tumor cells. Comparing cultivation medium of the drug, to count the cell quantity of each group after certain period of cultivation. Add normal cultivation medium with drug into the blank comparison group.

To classify the tumor - cell bearing cultivation bottles into drug - test group and comparison group, and add certain concentration of cultivated medium into them. Count cell quantity at different times. Add normal cultivated medium without drug content into the blank comparison group.

/18

V. Observation Criteria

Use the cell - growth control rates versus different drug dosages to make the drug control curve, and a curve for drug concentration versus control concentration (IC50). To make the time - cell - growth curve by observing the quantity of growth cells at difference times.

VI. Observation Time

Drug control curve: observation time for 4 days;

Cell growth curve: observation time for 7 days;

VII. Dosage Design

Tiandi heji to set up five dosage groups, respectively for 0.75, 3.75, 7.50, 18.75 and 37.5mg mg/ml (This drug has no control effect at gamma level).

VIII. Method of Drug feeding

Add the drug into the cultivation medium, and directly conduct cell cultivation; change cultivation medium every other day.

IX. Test Comparison

Blank comparison means normal cultivation medium without drug content.

Positive comparison adopts Ping Xiao Capsule, which is a medicine compound, black in color, 0.21g per capsule. It is made under the supervision of China Anti - Cancer Association, and produced by Shaanxi Xian State Pharmaceutical Plant, batch No. Shaan Wei Yao Zun Zi (1984) No. 00201, and provided by Shanghai Tumor Hospital. Ping Xiao Capsule is put into a bowl to be grinded into powder, and sterilize it under high pressure. Then dissolve Ping Xiao powder in the 15% calf serum cultivation medium, separate the solids centrifugally, and divide it into five dosage groups respectively for 0.3, 1.5, 3, 7.5 and 15mg/ml. The same drug feeding methods is as for Tiandi heji.

X. Test Result

The growth and reproduction of the four types of cultivated human tumor cells, i.e. Hela, 7704, 7901 and Al are able to be controlled by Tiandi heji depending on its dosage, while tumor cells without adding Tiandi heji are able to grow unlimitedly, and entered into logarithmic growth phase. See Table 16 for its off - body half - inhibition concentration. Also see Table 16 for the off - body half - inhibition concentration for Positive Comparison Group that uses Ping Xiao Capsule.

Table l6 Half - Inhibition Concentration on off - body tumor cell growth by Tiandi heji and Ping Xiao Capsule.

(IG50,X ± SD n = 3)

/19

Cell Strain	Tiandi heji	Ping Xiao Capsule

	(mg/ml)	(mg/ml)
Hela	3.74 ± 1.82	4.11 ± 1.24
7704	4.36 ± 1.97	5.25 ± 2.09
7901	3.08 ± 2.33	3.70 ± 0.60
A1	2.02 ± 0.40	5.56 ± 2.59

Tiandi heji has inhibition function on the off - body cultivated human tumor cells (Hela, 7704, 7901 and A1), and the off - body half - inhibition concentration (IG50) is 2 - 5mg/ml.

Acute toxic Test on the anti - tumor traditional Chinese medicine (Tiandi Heji) in this invention:

I. Purpose of Test:

To study the acute toxic reactions from one - time feeding of Tiandi heji to animals, and to calculate the half - inhibition fatal dosage LD50 at the same time.

II. Tested Medicine

Name: Tiandi heji.

Provided by: Shanghai Tiankang Pharmaceutical Plant

Labeled Amount: 0.75g crude drug per ml.

Preparation method: use the original solution without dilution.

Solvent: N/A

III. Animal: mouse

Source, breed, type, certificate: provided by Shanghai Lab Animal Center under the Chinese Academy of Sciences, CAS Shanghai N - 94Q,Kunming Breed.

Weight: 18 - 22g (6 years full age). Stop feeding for 16 hours (not including water).

Animal count: 40, group randomly, 10 in each group, half male and half female.

IV. Testing Method

Drug - feeding approach same as for clinic oral intake, and use stomach lavage (ig) on animal test.

Set up four dosage groups per LD50 statistical requirements, the dosage scale is at 0.2ml/20g.

The volume of dosage at a time shall be respectively 0.2 ml, 0.4ml, 0.6ml and 0.8ml/mouse; the maximum ig volume is at 0.8ml/mouse per New Drug (traditional Chinese medicine) Research Guidance.

Do not use solvent for the concocted drug solution.

Abnormal animal reactions: no obvious toxic reaction at small dosage; when use big dosages, the mouse first demonstrated increased excitement in activity, followed by weakened limbs, loose hair and inactivity, recovery in 4 - 6 hours. At dosage of 30ml/kg, one animal died 3 hours after ig; immediate anatomy showed gastric perforation, and the remaining drug liquid in the abdominal cavity proved that it did not die from the drug. The remaining animals were observed for 7 days without fatality, and not able to test LD50.

V. Result:

No obvious toxic reaction after small dosage feeding of this medicine; after feeding bigger dosages, the mouse first demonstrated excitement in activity, followed by weakened limbs, unsteady standing, loose hair and inactivity, but recovered in 4 - 6 hours, and completely recuperated in 24 hours.Observation:

No animal fatality in 7 days. (see Table 17) normal weight growth of the animal after drug feeding (see Table 18).

Table 17 Fatality Status after Acute Toxin ig of Tiandi heji

Dosage ml/kg	Animal Count Unit	Fatality Status										Test Result	
		0h	3h	6h	24h	48h	Day 3	Day 4	Day 5	Day 6	Day 7	Dead	Survived
10	10	0	0	0	0	0	0	0	0	0	0	0	10
20	10	0	0	0	0	0	0	0	0	0	0	0	10
30	10	0	0	0	0	0	0	0	0	0	0	1*	9
40	10	0	0	0	0	0	0	0	0	0	0	0	10

Note:*Fatality not attributed to drug - use.

Table 18 Weight Change in mouse before and after taking Tiandi hejii.

Dosage ml/kg	Times ig	animal count Unit	Pr e - medication X ± SD	Post - medication X ± SD
40	1	24	19.9 ± 1.3	25.6 ± 1.4
80	2	24	19.9 ± 1.6	23.6 ± 1.2
120	3	24	19.5 ± 1.4	23.6 ± 1.7*

Note: * average value for 22 animals

IV.Conclusion

Tiandi heji (Heaven and earth mixture) is of very little toxicity, the max tolerance for a mouse without death after ig is 40ml/kg; while the ig dosage of twice a day for not being

dead is 80ml/kg. The main performance after taking the medicine is quietness, less motion, general fatigue, loosened fir and feces becoming softer, which can all be restored to original states after withdrawal of the medicine.

The max tolerance test of this invention of anti - tumor traditional Chinese medicinal preparation (tiandi heji):

I. Objective of the test:

With a view to knowing the acute toxic reaction of an animal after being given the tiandi heji and to determining the max tolerance of an animal to the tiandi heji o

II. Medicine to be tested with

Name: Tiandi (Heaven and earth) mixture

Supplier unit: Shanghai Tiankang Pharmaceutical Factory

Nominal content of the preparation: 0.75g contained in each ml.

Dispensing method: use the original medicine liquid, which has not been diluted.

Solvent: No solvent has been used.

III.Animal: mouse

Source, species, strain and pass certificate: being provided by the Chinese Academy of Sciences Shanghai Experimental Animal Center, No.ZKH N - 94 - Q, Kunming Species mouse

/22

Weight: 18 - 22g (full 6 year age), fasting for 16 hours (being not deprived from water).

Quantity of animals: 72 pieces, divided into 3 average groups, each group being of 24 pieces, half female and half male

IV. Test method

Dosing channel: gastric irrigating (ig) being consistent with the monitored oral taking

Medicine feeding dosage: original medicine liquid of 40ml/kg tiandi heji, equal to 30ml/kg dried medicinal herbs

Since this product is a compound traditional Chinese medicine, which cannot be concentrated, so the original medicine is directly used; according to the provisions of the new medicine (traditional Chinese medicine) research guide, each time ig max volume dose for a mouse is 0.8ml/20g

Therefore, multiple dosing is selected

Abnormal reaction of the animal: after being ig dosed with tiandi heji, the animals present a slight excitement, their walking is increased, and immediately becoming of general fatigue, with motion being decreased and fir loosened.Those in the group dosed once a day are recovered in 4 - 6 hours; those in the group dosed twice ig a day decrease their motion, with fir loosened and being of general fatigue and feces becoming wet and softened; those in the group dosed three times of ig a day decrease their motion, with their fir being loosened and being of general fatigue and feces becoming wet and softened, some of the animals are of loose stool, and two in this group are found dead after 24 hours and 72 hours respectively; then they are dissected immediately, gastric mucosa is found defective, gastric wall is of blood stasis and intestinal is aerated; no other abnormalities are found; other animals under seven - day observation are found being of no death.

The clinic commonly - used dosage of tiandi heji is intended to be 30ml/person. Personal average weight is 60kg, the dosage for a person a day is 0.5ml/kg.The 40ml/kg/day ig for a mouse is equal to a 80 - times dosage for a man (80÷0.5 = 160) ; 120ml/kg/day is

equal to 160 times the dosage for a man (80÷0.5 = 160) ; 120ml/kg/day is equal to 240 times the dosage for a man (l20÷0.5 = 240).

V. Result:

After being fed with tiandi heji, the animals immediately present quietness, decrease motion, not gather together any longer, become fir loosened, and stay from each other with their feces becoming softer. Part of the animals become of general fatigue, lie prostrate on the ground, and continue for 2 - 3 hours and recover. Those under 40ml/kg/day feeding once a day and under 80ml/kg/day feeding twice a day are both found of no death. Two of those under 120ml/kg/day feeding thrice a day are found dead each after 24 hours and 72 hours respectively after medicine feeding, with the others being of normal motion and without eye - seen toxic symptom for seven days running. The dead animals were dissected immediately, gastric mucosa was found defective, gastric wall was of blood stasis and intestinal was aerated; no other abnormalities are found. When the experiment is concluded, their weight is increased at various extents. For the variation in weight before and after medicine feeding please see Table 2, they are of normal growth.

/23

The toxic test of this invention of anti - tumor traditional Chinese medicine preparation (tiandi heji) with SD big mice after their taking the medicine orally for 8 weeks

I. Test method:

60 SD big mice, half female and half make, are divided into three groups randomly, of which two are 20, 30ml/kg/day dosage groups and one is a reference group fed with distilled water. Twice a day of ig for 8 weeks running

II. Test conclusion:

1, After 8 weeks of tiandi heji ig, the big mice in 30ml/kg/day medicine fed group, after being fed with the medicine for 1 week, perform relatively excited and are fond of motion, running in the cage restlessly, and tend to be quiet after 10 minutes. From the third week on after being fed with the medicine, individual big mice are found with brown thin soft feces. And the symptom disappears after the medicine withdrawal.

The 20ml/kg/day group was found with no reaction. That shows that there is a certain relation between the symptom and the medicine dosage.

2, The weight of the big mice in groups with various tiandi heji dosages for 8 weeks was found increased, with the same growth curves. The males and females of the 20ml/kg/day were of fast weight increase, with a remarkable difference ($P < 0.05$).

The male mice of 30ml/kg/day group were found to take less food starting from the fourth week, with slow weight increase, in remarkable difference. The male mice in that group took much more food after the medicine withdrawal, with weight increasing rapidly. The weight of recovery groups was about the same, with no marked difference.

3, During the dosing period, part of the female mice in the 20, 30ml/kg/day groups were found with increase of adrenal cortex fascicular zone fatty cells, whether or not that the medicine can lead to the stress reaction of the female mice, recovery was witnessed after the medicine withdrawal.

During the recovery period, the organ coefficient ration of spleen of the female mice of the 20ml/kg/day group is remarkably lower than that of those of the 30ml/kg/day group, but in the histological examination the spleen white pulp was not seen of remarkable atrophic. Through the hematological, blood biochemical and pathological histology

examinations, no functional or histopathology toxic semantic variation of dose - dependent relation was found.

By summarizing the above - mentioned, there was no abnormal reaction seen with the 20ml/kg group after the tiandi heji ig was practiced for 8 weeks, which indicates that it is the non - toxic dosage group. The weight of the male mice in the 30ml/kg group increased rather slowly. After the medicine withdrawal they return to take food with their weight increasing greatly and liver and kidney functioning normally, and there was no toxic variation related to dosage appearing in the histopathology. So the dosage of 30ml/kg/day and below are regarded as basically safe dosage for big mice.

/24

The result of the stability test of this invention of anti - tumor traditional Chinese medicinal preparation (tiandi heji) is as follows:

Batch numbers of samples: three batches in total of Numbers of 1, 2 and 3

Inspection method: preserved at 37—40℃ and relative humidity of 75%, in glass bottle, sealed.

Inspection durations of time: 0 months, 1 month, 2 months and 3 months.

Inspection indexes: properties, identification, relative density, PH value and ether - soluble substances

Inspection result: see Table 19 below

/25

Table 19 Stability Test

Batch No.	Date	Properties	Identification ①	Identification ②	Ether - soluble substances%	PH value	Relative density

	0 months	Conforming to prescription	Positive reaction	Positive reaction	1.00	4.87	1.032
	1 month	Conforming to prescription	Positive reaction	Positive reaction	1.09	4.84	1.024
1	2 months	Conforming to prescription	Positive reaction	Positive reaction	0.94	4.87	1.025
	3 months	Conforming to prescription	Positive reaction	Positive reaction	0.94	4.76	1.026
	0 months	Conforming to prescription	Positive reaction	Positive reaction	1.11	4.86	1.024
	1 month	Conforming to prescription	Positive reaction	Positive reaction	1.10	4.89	1.022
2	2 months	Conforming to prescription	Positive reaction	Positive reaction	1.12	4.83	1.024
	3 months	Conforming to prescription	Positive reaction	Positive reaction	0.97	8.89	1.024
	0 months	Conforming to prescription	Positive reaction	Positive reaction	1.07	4.86	1.026
	1 month	Conforming to prescription	Positive reaction	Positive reaction	1.08	4.87	1.026
3	2 months	Conforming to prescription	Positive reaction	Positive reaction	1.00	4.86	1.026
	3 months	Conforming to prescription	Positive reaction	Positive reaction	1.08	4.81	1.027

/26

The above - mentioned result indicates that this invention of anti - tumor traditional Chinese medicinal preparation (tiandi heji) is either of anti - tumor effect, or of strengthening of immunologic function, which is in conformity to the eliminating evil factors and supporting healthy energy expounded by the traditional Chinese medicine.The preparation is of especially marked efficacy for heteroplastic molds of human body gastric cancer and liver cancer, and is of relatively good curative effect for mammary cancer, bone cancer, skin cancer, brain tumor and lung cancer; it is of a coordinating effect in combination with chemical therapy, and is of low toxicity as well, without leukocyte reducing effect and liver - kidney function disordering, which enables

it to be used in clinic purpose for long period of time. In case of expanding the human dosage to 80—240 times, no toxic side reaction is found, while the anti - tumor rate reaches 80% and above (the State standard stipulates 30%), which is 5—6 times higher than the existing traditional Chinese medicine of "Pingxiaopian", so it shows broad prospects for curing cancers.

The other purpose of this invention is to provide the preparation method of the above - mentioned anti - tumor traditional Chinese medicine, which method is to take the traditional Chinese medical herb in pieces of a recipe volume and powder it to 6 - 8 mesh, then add 10 - time alcohol to soak it for 24 hours, and heat it under reflux for 1 hour. After being filtered, it is to be added to with 8 - time alcohol and heated under reflux for 1 hour; after being filtered, the decoction dregs is to be cleaned with alcohol and to be pressed; then merge the filtered liquids of the two filtration and the squeezed liquid to carry out the film concentration, and gently add 1 to 3 times of alcohol during the concentration course; collect the concentrated liquid and recycle the alcohol, then reduce pressure to have a alcohol content of <4%, add in 0.06 times alcohol with 1% benzoic acid content, blend them uniformly, which may be bottled to manufacture the heji or be vacuum concentrated into dried plaster through routine method; which is to be powdered finely and being added in with forming agent as well as proper volume of 95% alcohol to be prepared into soft material; after being dried, the prepared granules are added in with lubricant agent, then put in bags to prepare them into dissolvable preparation or pressed into tablets to be put in gel capsules to be made into capsule preparations.

The auxiliary agent for serving as binder in the above - mentioned traditional Chinese medicine is starch, sugar powder or syrup, the disintegrant in it is CM - cellulose or

microcrystalline cellulose, the wetting agent in it is alcohol, the lubricant in it is magnesium stearate or talcum powder, and the preservative in it is benzoic acid.

Example 1: Preparing of anti - tumor traditional Chinese medicine of heji (tiandi heji)

(I) Recipe:

Mormordica cochinchinonsis 150g Gynocardia odorata 150g Pangolin scales 150g

/27

Rhubarb 150g Sweet root 150g Bamboo shavings 150g

Alcohol Proper volume

(II) Preparation method

Take the above five medicinal herbs in pieces in a 10 - time volume each, powder them to 6 - 8 mesh (about the size of green beans), add 25000ml alcohol in, mix then uniformly and close them tightly for soaking them for 24 hours. Through twice reflux at 85 - 89℃ each respectively, have them filtered, clean and squeeze the medicine dregs, combine the two filtration liquids and squeezed liquid, to carry out the film concentration, add in 1000ml of alcohol gently during the concentration, collect the concentrated liquid and recycle the alcohol, to make the volume proportion being 1 : 0 : 9, then through reduced - pressure concentration at 75 - 80℃0.08MPa to concentrate it to 9500ml,measure the alcohol volume (lower than 4%), then, when it remains hot, add 500ml 95% alcohol with 1% of benzoic acid in, to make the total volume being 10000ml, mix them uniformly, put them in quietness for 24 hours, centrifugalize them when they are cooled, discard sediment, integrate it with centrifugalized liquid and heat them at 60℃ for 1 hour, mix

them and cool them till below 30℃ and below, distribute them into 100ml brown bottles and the medicine is prepared.

Example 2: Preparing of anti - tumor traditional Chinese medicine of heji (tiandi heji)

Recipe: Mormordica cochinchinonsis 50g Gynocardia odorata 30g Rhubarb 50g Sweet root 150g Pangolin slices 20g Bamboo shavings 50g

The preparation method is the same as of Example 1.

Example 3: Preparing of anti - tumor traditional Chinese medicine of heji (tiandi heji)

Recipe: Mormordica cochinchinonsis 150g Gynocardia odorata 150g Rhubarb 200g Sweet root 250g Pangolin slices 160g Bamboo shavings 200g

The preparation method is the same as of Example 1.

Example 4: Preparing of anti - tumor traditional Chinese medicine of heji (tiandi heji)

Recipe: Mormordica cochinchinonsis 90g Gynocardia odorata 90g Rhubarb 100g Sweet root 125g Pangolin slices 80g Bamboo shavings 100g

The preparation method is the same as of Example 1.

Example 5: Preparation of tiandi heji

Recipe:

Mormordica cochinchinonsis 150g Gynocardia odorata 150g Pangolin 150g

/28

Rhubarb 160g sweet root 150g

Preparation method: among the above medicines, take the mormordica cochinchinonsis kernel with the shell removed, and mix it with the other medicines and powder them coarsely, add in 55% alcohol to soak the medicines for 24 hours, heated them under reflux for 1 hour, filter them to have the liquid for standby application; the medicine

dregs will be added in with 55% alcohol for once more reflux, the liquids extracted from the two soakings are to be filtered and film - concentrated with alcohol recycled, the concentration is to be continued till to the prescribed volume, which is to be filtered, with distilled water added to regulate it to the total volume of 1000ml and the medicine is prepared.

Example 6: Preparing of anti - tumor capsules

Recipe :

Mormordica cochinchinonsis 150g Gynocardia odorata 150g Pangolin 150g

Rhubarb 150g sweet root 150g

Preparation method: Prepare the medicine liquid in compliance with the method of Example 1, vacuum - concentrate the prepared medicine liquid into dried paste,

Powder it finely, add in forming agent and proper volume of 95% alcohol to prepare it into soft material, which is to be made into granules and put the granules into gel capsules after they dried.

Example 7: Preparing of anti - tumor tablets

The recipe is the same as that of Example 6.

Preparing method: prepare granules in compliance with Method 6 and make them into tablets after they are dried with the auxiliary material being added in

Example 8: Preparing of anti - tumor dissolvable preparation

The recipe is the same as that of Example 6.

Preparation method: Prepare the dissolvable preparation through the preparing of the dried granules in compliance with the method of Example 6 and adding auxiliary material in the granules after they are dried.